REMARKS

This amendment corrects errors in the text. Entry is respectfully solicited.

This amendment is submitted prior to or concurrently with the payment of the issue fee and, therefore, no petition or fee is required. No new matter has been added.

Drawings:

Although the Notice of Allowability does not indicate that formal drawings are required, the applicants herewith submit formal drawings. The formal drawings delete text that was inadvertently entered with the current figures, for example, the text description under FIG. 36.

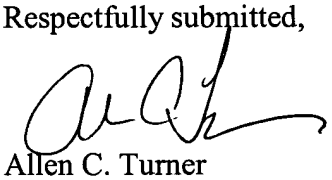
Priority Documents:

Enclosed herewith are certified copies of the priority documents EP98201695.8 filed 20 May 1998 and EP98202706.2 filed 12 August 1998.

Supplemental Declaration:

The applicants herewith submit a Supplemental Declaration, which corrects inadvertent errors in the filing dates of the priority documents. Two of the inventors are currently unavailable, therefore, an additional Supplemental Declaration will be submitted when it becomes available.

Respectfully submitted,



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IN THE SPECIFICATION:

Please replace the first paragraph inserted by Preliminary Amendment on November 20, 2000, with the following:

Related Applications: This application is a continuation of co-pending International Application No. PCT/NL99/00313, filed May 20, 1999, designating the United States of America~~, which itself claims priority from EP 98201695.8, filed on May 20, 1998, and EP 98202706.2, filed on August 12, 1998.~~

Please replace the paragraph following the subheading "Anti-shock activity of IR-U/LMDF, IR-P3, AR-A3:" on page 69, with the following:

Lower molecular weight fractions of IR obtained by purification method 2 (IR-U/LMDF), ~~had~~ also had anti-shock activity (figure 57) and mice treated with this fraction remained alive. We also tested ~~also~~ all three fractions obtained from ~~superdex@peptide~~ the superdex™ column, IR-U/LMDF, IR-P3, and IR-A3, for anti-shock activity. ~~Method~~ The method for this activity screening is mentioned elsewhere in this document. Our results showed that all three fractions from ~~superdex@peptide~~ the superdex™ column and IR-P3 had anti-shock activity, while IR-A3 had low to moderate activity (data not shown).

Please replace the first full paragraph on page 109 with the following:

Figure 29-31. In order to know whether IR has also effect on the maturation of DC, BM from NOD mice were also directly co-cultured with GM-CSF and IR for 7 days. At day 8 all cells were analyzed by a flow cytometer for ~~experssion~~ expression of the following markers: CD1d, CD11c, CD14, CD31, CD40, CD43, CD80, CD86, CD95, ER-MP20, ER-MP58, F4/80, E-cad, MHC II, MHC I, RB6 8C5. We observed that all DC treated with IR were less mature ~~then~~ than control DC treated with GM-CSF only. This was concluded from the decrease in cell surface markers CD1d, ER-MP58, F4/80, CD14, and the increase in CD43, CD95, CD31 and

E-cad. Moreover no change was observed in cell surface markers ER-MP20/LY6C, MHC I and II (~~figure 29~~figures 29A and 29B). ~~Figure 30 and 31. shows~~ Figures 30A, 30B and 31 show, when DC were cultured with GM-CSF for 6 days and at day 7 co-cultured with 30 IU/ml IR-P (figure 30) or 100 mg/ml of IR-U/LMDF (figure 31) for additional 24 hrs, the DC became more mature and could function better as APC. This was concluded from the increase in CD1d, CD40, CD80, CD86, CD95, F4/80, CD11c and MHC II cell surface markers (figures ~~30~~30A, 30B and 31).